REMARKS

Claims 1 to 15 are pending. In the present communication, claim 14 has been canceled and claims 1 and 13 have been amended. Support for the amendments to claim 1 can be found, for example, in the specification on page 4, lines 6-20 and page 8, lines 18-19. A marked up version to show changes made is attached herewith as Exhibit A; and the claims as they will stand upon entry of the amendments is attached herewith as Exhibit B.

The amendments submitted herewith are supported by the specification and original claims and do not add new matter. The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicants' invention more clearly. It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable. Since the amendments do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendments is respectfully requested.

Double Patenting

Claims 1-11 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-11 of U.S. Patent No. 5,814,500. In response, a terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) to overcome the rejection is submitted herewith.

Rejections Under 35 U.S.C. § 112

The rejection of claims 13-15 under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement is respectfully traversed.

Applicant respectfully disagrees with the Examiner's assertion that the specification does not provide enablement for the breadth of nucleic acid constructs and methods instantly claimed. Applicant's invention, as defined by claim 13 and claims dependent therefrom, recites a method for suppression of gene expression in a cell comprising administering to the cell a suppressive-effective amount of a nucleic acid construct. Applicants respectfully submit that the specification provides adequate guidance to practice invention methods. However, in order to facilitate prosecution of the present application and reduce the issues on appeal, claim 13 has been amended to recite administration to the cell *in vitro*.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 13 to 15 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102

The rejection of claims 1 to 12 under 35 U.S.C. § 102(a) as allegedly being anticipated by Michienzi *et al.* (Proc. Natl. Acad. Sci. USA, 993:7219 (1996); hereinafter "Michienzi") is respectfully traversed.

Applicant's invention distinguishes over the prior art by reciting a nucleic acid construct for suppressing gene expression comprising an unmodified 5' stem loop structure, an antisense nucleic acid, and an unmodified 3' stem loop structure, wherein the stem loop structures flank the antisense nucleic acid. In contrast, Michienzi teaches nucleic acid constructs in which the stem loop III of U1 snRNA is modified by the addition of a hammerhead ribozyme within the actual stem loop structure.

Accordingly, all constructs taught by Michienzi. contain modified stem loop structures, wherein Applicant's constructs contain unmodified stem loop structures.

Applicants respectfully disagree with the Examiner's assertion that the "unmodified" construct of Michienzi contains unmodified stem loops. The unmodified U1-Rz construct referred to by the Examiner on page 7219, column b, lines 39-42, is shown graphically in Figure 1. Michienzi's "unmodified" U1-Rz construct is a U1 snRNA that has a hammerhead ribozyme nucleic acid sequence inserted into the stem-loop III nucleic acid sequence. Michienzi's "modified" construct (U1-Rz_m) is a construct in which the nucleic acid sequence forming the catalytic core of the hammerhead, *i.e.*, CUGAUGA, has C replaced by G (see page 7220, column b, lines 26-32). Such modification renders the catalytic activity of the ribozyme inactive. Thus, the "unmodified" constructs of Michienzi have stem loop structures that are modified by the presence of ribozyme nucleic acid. They contrast with the "modified" constructs (U1-Rz_m) in which the ribozyme nucleic acid insert is itself modified. Michienzi does not teach any nucleic acid constructs having unmodified stem loop structures. Accordingly, Michienzi can not anticipate Applicant's invention.

In view of the above amendments and remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1 to 12 under 35 U.S.C. § 102(a).

Applicant submits that the pending claims are in condition for allowance. In the event any matters remain to be resolved in view of this communication, Examiner is requested to telephone Applicant's representative below, so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: **May 15, 2002**

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Enclosures: Exhibits A and B

In re Application of:
Harry C. Dietz
Application No.: 09/163,289
Filed: September 29, 1998
Exhibit A: Page 1

PATENT
Attorney Docket No.: JHU1400-1

EXHIBIT A: CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

Please amend the claims as follows:

1. (Twice Amended) A nucleic acid construct for suppressing gene expression comprising in 5' to 3' orientation:

an unmodified 5' stem loop structure;

an antisense nucleic acid; and

an unmodified 3' stem loop structure, wherein the antisense nucleic acid is flanked by the stem loop structures.

13. (Twice Amended) A method for suppression of gene expression in a cell comprising administering to the cell *in* vitro a suppressive-effective amount of the nucleic acid construct of claim 1, whereby expression of the gene is suppressed in the cell.

In re Application of:
Harry C. Dietz
Application No.: 09/163,289
Filed: September 29, 1998
Exhibit B: Page 1

PATENT
Attorney Docket No.: JHU1400-1

EXHIBIT B: CLAIMS AS THEY WILL STAND UPON ENTRY OF THE AMENDMENT

1. (Twice Amended) A nucleic acid construct for suppressing gene expression comprising in 5' to 3' orientation:

   an unmodified 5' stem loop structure;

   an antisense nucleic acid; and

   an unmodified 3' stem loop structure, wherein the antisense nucleic acid is flanked by the stem loop structures.

2. (Amended) The nucleic acid construct of claim 1, wherein the unmodified stem loop structures are unmodified U snRNA structures.

3. The nucleic acid construct of claim 2, wherein the U snRNA is U1.

4. The nucleic acid construct of claim 1, further comprising a promoter.

5. The nucleic acid construct of claim 4, wherein the promoter is a U1 snRNA promoter.

6. The nucleic acid construct of claim 4, wherein the promoter is a constitutive promoter.

7. The nucleic acid construct of claim 4, wherein the promoter is an inducible promoter.

8. The nucleic acid construct of claim 1, further comprising a ribozyme nucleic acid.

9. The nucleic acid construct of claim 8, wherein the ribozyme nucleic acid is located between the 5' and 3' stem loop structures.

10. The nucleic acid construct of claim 8, wherein the ribozyme nucleic acid is a hammerhead-type ribozyme.

11. The nucleic acid construct of claim 8, wherein a consensus sequence for ribozyme cleavage in a target nucleic acid is 5'-GUC-3' or 5'-GUA-3'.

12. The nucleic acid construct of claim 1, wherein the antisense nucleic acid is selected from the group consisting of rent-1, HPV E6, HIV, hyaluronic acid synthase, and fibrillin.

13. (Twice Amended) A method for suppression of gene expression in a cell comprising administering to the cell *in vitro* a suppressive-effective amount of the nucleic acid construct of claim 1, whereby expression of the gene is suppressed in the cell.

15. The method of claim 13, further comprising administering a modified nucleic acid encoding a wild-type polypeptide corresponding to the gene product of the gene being suppressed, wherein the modified nucleic acid is resistant to ribozyme cleavage and/or antisense inhibition.